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Original Research Article

Role of fetal pulmonary artery Doppler in prediction of neonatal respiratory distress in neonates of diabetic mothers

Hager Mamdouh G. Taha*, Nagwa Mahmoud Al Ghorab, Mohammed Mohsen Al-Namory, Naglaa Ali Hussein

Department of Obstetrics and Gynecology, Tanta University, Tanta, Egypt

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***Correspondence:**
Hager Mamdouh G. Taha,
E-mail: hagergadou23@gmail.com

ABSTRACT

Background: Newborn respiratory complication is one of the most prevalent and life-threatening disorders. The clinical indications of early newborn respiratory distress with consistent radiologic features. The Doppler examination of the primary pulmonary artery in the foetus has been proven to be beneficial. The foetal pulmonary artery At/Et ratio is linked to foetal gestational age and amniotic fluid foetal lung maturity (FLM) tests. The aim of the study was to assess the accuracy of foetal main pulmonary artery (MPA) Doppler indices in prediction of the development of neonatal respiratory distress syndrome (RDS) in diabetic mothers.

Methods: This was a prospective observational study carried out on 100 cases of diabetic mothers in obstetrics and gynecology department, Tanta University during one year from the approval of the university counsel. The physician evaluated the foetal heart in a methodical manner after a regular ultrasound assessment that included foetal biometry, anomaly scan, measured foetal weight, and amniotic fluid index. Classic chest radiological features include reticulogranular patterns, air bronchogram and ground glass look, as well as the need for surfactant.

Results: PI and RI were significantly higher in newborns with RDS than those without RDS (p=0.025 and 0.036 respectively) PSV and At/Et ratio were significantly reduced in neonates with RDS compared with RDS free ones (p=0.004 and <0.001 respectively). RI was significantly higher in neonates with RDS than those without RDS (P = 0.048) PSV and At/Et ratio were significantly reduced in newborns with RDS compared to RDS free ones (p=0.008 and <0.001 respectively). The ROC curve displayed that the cut off value of ≤0.25 for At/Et ratio was associated with a sensitivity of 76.92%, a specificity of 100.0%, a PPV of 100.0% and a NPV of 96.7% for prediction of neonatal RDS with AUC of 0.925 and p≤0.001.

Conclusions: development of neonatal RDS in foetus of diabetic mothers with a cut off value of ≤0.25, a sensitivity of 76.92%, a specificity of 100.0%, a PPV of 100.0%, a NPV of 96.7% and AUC of 0.925 The usage of corticosteroids improved the Doppler indices of main pulmonary artery and is accompanied by less morbimortality related to RDS.

Keywords: Fetal pulmonary artery, Doppler neonatal respiratory distress, Diabetic mothers

INTRODUCTION

The most prevalent cause of problems during pregnancy is maternal diabetes mellitus (DM), which includes gestational diabetes mellitus (GDM) and pre-gestational diabetes mellitus (PGDM).[1] In the United States (US), the incidence of GDM is estimated to be up to 9.2%, while the prevalence of PGDM is as high as 1%.[2] The prevalence of diabetes mellitus has been increasing in Egypt In 2014, over 7.5 million people (aged 20-79 years) were suffering from diabetes in Egypt and this number is expected to increase to 13.1 million by the year 2035 and Egypt diabetes prevalence was 20.9% in 2021.[3,4] DM in the mother raises the risk of cardiovascular disease (CVD) in her children and expectant moms.[5,6] Furthermore, maternal

DM is linked to a number of negative obstetric outcomes, including abnormalities, macrosomia, and newborn metabolic problems.[5] In addition, newborn respiratory complication is one of the most prevalent and life-threatening disorders. Since the early 1970s, a link has been shown between maternal DM and newborn respiratory distress syndrome (RDS).[7] Furthermore, elevated insulin levels block surfactant protein A, which delays lung development in diabetes moms' foetuses (SP-A) inhibition of the expression of the SP-A and SP-B genes causes an increase in the incidence of RDS in diabetic newborns.[8]

Many factors linked with foetal hemodynamics may be measured using the Doppler effect. These data have enabled the characterization of several vessels in the maternal-foetal circulatory system, allowing for the monitoring of mother and foetal health.[9] The Doppler examination of the primary pulmonary artery in the foetus has been proven to be beneficial in the investigation of the impedance of such vascular systems, and alterations in those variables have been shown to correlate with GA, foetal lung maturity, and neonatal outcomes.[10-13]

The aim of the study was to assess the accuracy of foetal main pulmonary artery (MPA) Doppler indices in prediction of the development of neonatal RDS in diabetic mothers.

METHODS

This was a prospective observational study carried out on 100 cases of diabetic mothers in obstetrics and gynecology department, Tanta University during one year from the approval of the university counsel. Based on sample size calculation, the present study was carried out on a total of 100 pregnant women in 3rd trimester suffering from DM.

Inclusions criteria

Age group: 20-40 years, singleton viable pregnancy, all females between 34 to 40 weeks of gestation, antenatal steroids and indicated for elective caesarean section.

Exclusion criteria

Intrauterine growth retardation, congenital anomalies of heart and lung, known foetal chromosomal abnormality, oligohydramnios, any maternal complications throughout their gestation: pre-existing hypertension, pregnancy-induced hypertension, preeclampsia, renal disease, receiving medication during the pregnancy apart from iron supplements Ca^{2+}, and insulin and free interval from Doppler assessment to labor more than three days.The included females were subjected to the following: history taking, clinical examination, laboratory investigations, Doppler examination of the foetal pulmonary artery. All ultrasound tests were done by a single examiner utilizing the Samsung Medison H60, Korea and 3.5 MHZ transabdominal probe.

The physician evaluated the foetal heart in a methodical manner after a regular ultrasound assessment that included foetal biometry, anomaly scan, measured foetal weight, and amniotic fluid index. The physician traced the MPA till midway between the pulmonary valve and the bifurcation of the right and left divisions in the axial view of the thorax, with the foetus at rest and no foetal breathing motions. The angle of insonation was kept at 15° and the pulsed Doppler sample gate was set at 3 mm. The Doppler gain and scale were adjusted for the best depiction of the PSV and early diastolic notch in the velocity waveform.

The Doppler waveform of the MPA had its typical shape. At the conclusion of the systole, a tiny notch of reversed flow may also be detected. The MPA waveform has a distinct shape that distinguishes it from the ductus arteriosus wave, which is rounder, fuller, and triangular in shape with more diastolic flow. Diagnosis of RDS: classic chest radiological features include reticulogranular patterns, air bronchogram and ground glass look, as well as the need for surfactant

Statistical analysis

SPSS version 27 (IBM©, Chicago, IL, USA) for Windows was utilized to evaluate the data Quantitative data was reported as mean SD or median (range) according to normality, whereas qualitative data was expressed as number and percentage. According to the nature of the data, the relevant statistical tests were employed A were judged statistically significant (p value≤0.05).

RESULTS

This study was performed on a total of 100 pregnant females in 3rd trimester suffering from diabetes mellitus (DM). The study participants were then subdivided into two groups: (a) neonates with RDS (n=13); and (b) neonates without RDS (n=87). Age, gestational age by LMP, gravidity, parity and HbA1c were insignificantly different between neonates with RDS and RDS free ones (Table 1). PI and RI were significantly higher in newborns with RDS than those without RDS (p=0.025 and 0.036 respectively) PSV and At/Et ratio were significantly reduced in neonates with RDS compared with RDS free ones (p=0.004 and <0.001 respectively) (Table 2). RI was significantly higher in neonates with RDS than those without RDS (p=0.048) PSV and At/Et ratio were significantly reduced in newborns with RDS compared to RDS free ones (p=0.008 and <0.001 respectively) (Table 3).

The ROC curve displayed that the cut off value of >7 for SD was associated with a sensitivity of 53.85%, a specificity of 60.92%, a PPV of 17.1% and a NPV of 89.8% for prediction of neonatal RDS with AUC of 0.545 and p=0.622.The ROC curve displayed that the cut off value of >2 for PI was associated with a sensitivity of 100.0%, a specificity of 34.48%, a PPV of 18.6% and a NPV of 100.0% for prediction of neonatal RDS with AUC

of 0.668 and p=0.025. The ROC curve displayed that the cut off value of >0.87 for RI was associated with a sensitivity of 53.85%, a specificity of 89.66%, a PPV of 43.7% and a NPV of 92.9% for prediction of neonatal RDS with AUC of 0.655 and p=0.152. The ROC curve displayed that the cut off value of >0.87 for PSV was associated with a sensitivity of 100.0%, a specificity of 43.68%, a PPV of 21.0% and a NPV of 100.0% for prediction of neonatal RDS with AUC of 0.719 and p=0.001. The ROC curve displayed that the cut off value of ≤0.25 for At/Et ratio was associated with a sensitivity of 76.92%, a specificity of 100.0%, a PPV of 100.0% and a NPV of 96.7% for prediction of neonatal RDS with AUC of 0.925 and p≤0.001 (Table 4).

Table 1: Patients' characteristics in both studied groups.

Variables		Neonates with RDS (n=13) (%)	Neonates without RDS (n=87)	P value
Age (years)	Mean±SD	29.38±6.32	28.49±5.99	0.62
	Range	20-38	20-39	
Gestational age at delivery by LMP (weeks)	Mean±SD	35.3±1.49	35.76±1.12	0.199
	Range	34-38	37-40	
Gravidity	1	1 (7.7)	16 (18.4)	0.242
	2	5 (38.5)	24 (27.6)	
	3	6 (46.2)	24 (27.6)	
	4	1 (7.7)	23 (26.4)	
Parity	0	1 (7.7)	20 (23.0)	0.354
	1	5 (38.5)	23 (26.4)	
	2	6 (46.2)	28 (32.2)	
	3	1 (7.7)	16 (18.4)	
HbA1c (%)	Mean±SD	7.52±0.82	7.15±0.69	0.081
	Range	6.3-9.7	5.9-9.4	

Note: LMP: last menstrual period; *-statistically significant as p value<0.05.

Table 2: Pulmonary artery indices before corticosteroids in both studied groups.

Variables		Neonates with RDS (n=13) (%)	Neonates without RDS (n=87)	P value
S/D	Mean±SD	6.96±0.42	6.90±0.4	0.598
	Range	6.3-7.5	6.1-7.2	
PI (cm/s)	Mean±SD	2.31±0.20	2.18±0.19	0.025*
	Range	2.1-2.7	1.9-2.5	
RI (cm/s)	Mean±SD	0.82±0.12	0.76±0.08	0.036*
	Range	0.64-0.97	0.62-0.9	
PSV (cm/s)	Mean±SD	62.77±5.93	67.95±5.88	0.004*
	Range	53-70	58-77	
At/Et ratio	Mean±SD	0.25±0.05	0.35±0.04	<0.001*
	Range	0.18-0.34	0.28-0.41	

Note: *-Statistically significant as p value<0.05; S/D: systolic diastolic ratio, PI: Pulsatility index; RI: Resistance index; PSV: Peak systolic velocity; At:Et ratio: Acceleration time to ejection time ratio.

Table 3: Pulmonary artery indices after corticosteroids in both studied groups.

Variables		Neonates with RDS (n=13) (%)	Neonates without RDS (n=87)	P value
S/D	Mean±SD	6.96±0.42	6.90±0.4	0.598
	Range	6.3-7.5	6.1-7.2	
PI (cm/s)	Mean±SD	2.04±0.22	2.18±0.19	0.051
	Range	1.74-2.42	1.9-2.5	
RI (cm/s)	Mean±SD	0.74±0.12	0.76±0.08	0.048*
	Range	0.57-0.92	0.62-0.9	
PSV (cm/s)	Mean±SD	55.46±5.85	67.95±5.88	0.008*
	Range	46-63	58-77	

Continued.

Variables		Neonates with RDS (n=13) (%)	Neonates without RDS (n=87)	P value
At/Et ratio	Mean±SD	0.28±0.05	0.35±0.04	<0.001*
	Range	0.18-0.34	0.28-0.41	

Note: *-Statistically significant as p value<0.05; S/D: systolic diastolic ratio, PI: Pulsatility index; RI: Resistance index; PSV: Peak systolic velocity; At:Et ratio: Acceleration time to ejection time ratio.

Table 4: Accuracy of pulmonary artery indices in prediction of neonatal RDS.

Variables	Cutoff	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
S/D	>7	53.85	60.92	17.1	89.8
PI (cm/s)	>2	100.0	34.48	18.6	100.0
RI (cm/s)	>0.87	53.85	89.66	43.7	92.9
PSV (cm/s)	≤70	100.0	43.68	21.0	100.0
At/Et ratio	≤0.25	76.92%	100.0	100.0	96.7

Note: *-Statistically significant as p value<0.05; S/D: systolic diastolic ratio, PI: Pulsatility index; RI: Resistance index; PSV: Peak systolic velocity; At:Et ratio: Acceleration time to ejection time ratio.

DISCUSSION

RDS is considered one of the main etiologies of infant respiratory failure and death.[13] RDS was thought to be mostly present in preterm babies.[14] RDS is becoming more commonly diagnosed in term infants due to increased awareness.[15]

Premature births can occur naturally or as a result of PROM; nevertheless, preterm deliveries are often induced by the physician premature births can occur inadvertently due to gestational age (GA) errors, which are prevalent in women who have an ECS.[16]

Given the significance of RDS as an etiology of infant morbimortality in late preterm and early term births, assessing FLM prior to labor seems reasonable.[17] The use of corticosteroids during pregnancy hastens lung maturation. The typical weakening of the double capillary loops, which results in the thin gas-exchanging walls of alveoli, is accelerated, leading in rapid alveolisation. The development of type II pneumocytes that produce surfactant is also accelerated. Despite the fact that corticosteroids cause alveolization to begin quickly.[18] Type II pneumocytes create pulmonary surfactant Surfactant phospholipids help to reduce surface tension, whereas surfactant proteins help to regulate surfactant activity and may potentially have an immunomodulatory role.[19]

The Doppler examination of the primary pulmonary artery in the foetus was proven to be beneficial in the investigation of the impedance of the vascular systems, and alterations in those variables are displayed to correlate with GA and FLM, as well as neonatal outcomes.[10-13] The foetal pulmonary artery At/Et ratio has been linked to foetal GA and amniotic fluid foetal lung maturity (FLM) tests.[13] Kim et al investigated whether the At/Et ratio of the foetal MPA Doppler waveform may predict the outcomes of foetal lung maturity tests in amniotic fluid.[11] They discovered that newborns with RDS had lower Apgar scores at 1 min and 5 min than those who did not have RDS. Moety et al explored whether foetal MPA Doppler indices could predict the development of newborn RDS in 698 suitable foetuses delivered within 24 hours and discovered 55 (7.87%) suffered neonatal RDS.[13] They found that foetuses with newborn RDS had considerably lower At/Et and PSV, as well as greater PI and RI, as compared to foetuses who did not acquire RDS. This indicates that foetuses with RDS have higher pulmonary vascular resistance and pressure, as well as lower pulmonary blood flow, than those who do not.

According to our findings, Guan et al revealed alterations in the foetal MPA Doppler waveforms during gestation and evaluated their prognostic potential for newborn RDS.[12] They discovered that the At/Et of the MPA was considerably lower in preterm foetuses with RDS. Chaoui et al characterized typical blood flow velocity waveforms in the major divisions of the right and left pulmonary arteries in the human foetus and established reference ranges for several Doppler parameters throughout the second 1/2 of pregnancy.[20] A total of 86 normal singleton foetuses aged 18 to 38 weeks were involved in the study.

The researchers discovered that infants with RDS had lower levels of AT/ET. Lindsley et al compared the blood flow of the MPA in pregnant females at risk for PTB who were managed with steroids to an uncomplicated cohort who were not on steroid medication. They discovered that foetuses given corticosteroids had a considerably shorter pulmonary artery acceleration time than those who were not.[21] In addition, Moety et al demonstrated that a cut off value of 0.305 for At/Et might expect the development of neonatal RDS in a foetus delivered between 34 and 38±6 weeks with a sensitivity of 76.4 percent and a specificity of 91.6%, with an AUC/ROC of 0.899, with a sensitivity of 76.4 percent and a specificity of 91.6%.

Furthermore, as compared to At/Et, the capacity of PI and RI to predict RDS development showed lesser sensitivity and specificity, as we observed in our study.[13] In addition, Schenone et al investigated whether the foetal main pulmonary artery Doppler waveform's

acceleration/ejection time ratio may reliably predict the outcomes of foetal lung maturity tests in amniotic fluid.[9] They looked at 43 pregnant women who were going to an ultrasound unit for clinically indicated foetal lung maturity testing. According to the ROC curve, a foetal MPA Doppler waveform cutoff of 0.3149 had a specificity of 93% (95% CI), a sensitivity of 73% (95%CI), a NPV of 87% (95%CI), and a positive predictive value of 85 percent (95%CI) for predicting immature surfactant.

CONCLUSION

Fetal MPA At/Et Doppler indices is considered an accurate method for prediction of the development of neonatal RDS in foetus of diabetic mothers with a cut off value of ≤0.25, a sensitivity of 76.92%, a specificity of 100.0%, a PPV of 100.0%, a NPV of 96.7% and AUC of 0.925 The usage of corticosteroids improved the Doppler indices of main pulmonary artery and is accompanied by less morbimortality related to RDS.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Cummings JJ, Gerday E, Minton S, Katheria A, Albert G, Flores-Torres J, et al. Aerosolized Calfactant for Newborns With Respiratory Distress: A Randomized Trial. Pediatrics. 2020;146(5):e20193967.
2. Parimi M, Nitsch D. A Systematic Review and Meta-Analysis of Diabetes During Pregnancy and Congenital Genitourinary Abnormalities. Kidney Int Rep. 2020;5(5):678-93.
3. Khattab M, Mahmoud K, Shaltout I. Effect of Vildagliptin Versus Sulfonylurea in Muslim Patients with Type 2 Diabetes Fasting During Ramadan in Egypt: Results from VIRTUE Study. Diabetes Ther. 2016;7(3):551-60.
4. AlSawahli H, Mpyet CD, Ezzelarab G, Hassanin I, Shalaby M, Safa O, et al. Population-based cross-sectional prevalence survey of diabetes and diabetic retinopathy in Sohag-Egypt, 2019. BMJ Open. 2021;11(6):e047757.
5. Haleluya N, Wainstock T, Landau D, Sheiner E. Maternal gestational diabetes mellitus and the risk of subsequent pediatric cardiovascular diseases of the offspring: a population-based cohort study with up to 18 years of follow up. Acta Diabetol. 2018;55(10):1037-42.
6. Sampson S, Paradis G, Healy-Profitós J, St-Pierre F, Auger N. Gestational diabetes and risk of cardiovascular disease up to 25 years after pregnancy: a retrospective cohort study. Acta Diabetol. 2018;55(4):315-22.
7. Li Y, Wang W, Zhang D. Maternal diabetes mellitus and risk of neonatal respiratory distress syndrome: a meta-analysis. Acta Diabetol. 2019;56(7):729-40.
8. Miakotina OL, Goss KL, Snyder JM. Insulin utilizes the PI 3-kinase pathway to inhibit SP-A gene expression in lung epithelial cells. Respir Res. 2002;3(1):27.
9. Schenone MH, Samson JE, Jenkins L, Suhag A, Mari G. Predicting fetal lung maturity using the fetal pulmonary artery Doppler wave acceleration/ejection time ratio. Fetal Diagn Ther. 2014;36(3):208-14.
10. Granstam SO, Björklund E, Wikström G, Roos MW. Use of echocardiographic pulmonary acceleration time and estimated vascular resistance for the evaluation of possible pulmonary hypertension. Cardiovasc Ultrasound. 2013;11:7.
11. Kim SM, Park JS, Norwitz ER, Hwang EJ, Kang HS, Park CW, et al. Acceleration time-to-ejection time ratio in fetal pulmonary artery predicts the development of neonatal respiratory distress syndrome: a prospective cohort study. Am J Perinatol. 2013;30(10):805-12.
12. Guan Y, Li S, Luo G, Wang C, Norwitz ER, Fu Q, et al. The role of doppler waveforms in the fetal main pulmonary artery in the prediction of neonatal respiratory distress syndrome. J Clin Ultrasound. 2015;43(6):375-83.
13. Moety GA, Gaafar HM, El Rifai NM. Can fetal pulmonary artery Doppler indices predict neonatal respiratory distress syndrome? J Perinatol. 2015;35(12):1015-9.
14. Koivisto M, Marttila R, Kurkinen-Räty M, Saarela T, Pokela ML, Jouppila P, et al. Changing incidence and outcome of infants with respiratory distress syndrome in the 1990s: a population-based survey. Acta Paediatr. 2004;93(2):177-84.
15. Bouziri A, Ben SS, Hamdi A, Menif K, Belhadj S, Khaldi A, et al. Acute respiratory distress syndrome in infants at term and near term about 23 cases. Tunis Med. 2007;85(10):874-9.
16. Menon R. Spontaneous preterm birth, a clinical dilemma: etiologic, pathophysiologic and genetic heterogeneities and racial disparity. Acta Obstet Gynecol Scand. 2008;87(6):590-600.
17. Tita AT, Landon MB, Spong CY, Lai Y, Leveno KJ, Varner MW, et alk. Timing of elective repeat cesarean delivery at term and neonatal outcomes. N Engl J Med. 2009;360(2):111-20.
18. Kemp MW, Jobe AH, Usuda H, Nathanielsz PW, Li C, Kuo A, et al. Efficacy and safety of antenatal steroids. Am J Physiol Regul Integr Comp Physiol. 2018;315(4):825-39.
19. Akella A, Deshpande SB. Pulmonary surfactants and their role in pathophysiology of lung disorders. Indian J Exp Biol. 2013;51(1):5-22.
20. Chaoui R, Taddei F, Rizzo G, Bast C, Lenz F, Bollmann R. Doppler echocardiography of the main stems of the pulmonary arteries in the normal human fetus. Ultrasound Obstet Gynecol. 1998;11(3):173-9.

21. Lindsley W, Hale R, Spear A, Adusumalli J, Singh J, DeStefano K, et al. Does corticosteroid therapy impact fetal pulmonary artery blood flow in women at risk for preterm birth? Med Ultrason. 2015;17(3):280-3.

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